Rejection Under 35 U.S.C. § 112, second paragraph

Applicants acknowledge the Examiner's withdrawal of the rejections, based on 35 U.S.C. § 112, of claims 1 and 3-7.

The Office has rejected claims 2 and 12 under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claims the subject matter which applicant regards as the invention." (*See* Office Action, p. 3.)

Applicants respectfully traverse. However, merely to expedite prosecution, Applicants have amended claims 2 and 12. Accordingly, the rejections should be withdrawn.

The Office has also rejected claims 8, 13 and 14 under § 112, second paragraph, because platelets are cytoplasmic fragments of megakaryocytes and, thus, are not hematopoietic cells. (*See* Office Action, p. 9.)

Applicants traverse. To expedite prosecution, however, Applicants have amended claims 8, 13 and 14 by deleting the term "platelets" and replacing it with the term "megakaryocytes." Applicants respectfully request the rejection be withdrawn.

Finally, the Office rejected claims 2-4, 8, 13 and 14 under 35 U.S.C. § 112, first paragraph, as containing subject matter not described in the specification in such a way as to enable one of ordinary skill in the art. The Office specifically states that since a platelet does not contain a nucleus, the transfected DNA construct would not be expressed in the platelet. (*See* Office Action, pp. 9-11.) As such, the specification does not enable one of skill in the art to express a DNA construct in platelets.

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Applicants have amended claims 8, 13 and 14 to recite "megakaryocytes." A megakaryocyte contains a nucleus. Thus, a DNA construct transfected into a megakaryocyte can be expressed. In light of this amendment, Applicants respectfully request the rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

Applicants acknowledge the Examiner's withdrawal of the rejection of claim 4 under 35 U.S.C. § 103(a) as being unpatentable over Hao, Uzan, and further in view of Kurachi.

The Office has maintained the rejection of claims 1, 5, 9 and 10-12 under 35 U.S.C. § 103(a) as "being unpatentable over Hao et al. (Human Gene Therapy (July 1995) 6: 873-880) in view of Uzan et al. (J. Biol. Chem. (1991) 266(14): 8932-8939)." (*See* Office Action, p. 4.)

As set forth in M.P.E.P. § 2143.01, in order to establish a *prima facie* case of obviousness the Office must meet three criteria. "First, there must be some suggestion or incentive, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations." (M.P.E.P. § 2143.01 and cases cited therein.)

As explained below, the Office has failed to establish a *prima facie* case of obviousness because one of skill in the art would not be motivated to combine the teachings of Hao and Uzan. Further, the skilled artisan would not reasonably expect to succeed in expressing factor IX in hematopoietic cells using a hematopoietic-specific promoter if he were to combine Hao and Uzan. Accordingly, the rejection should be withdrawn.

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Assuming *arguendo* that Uzan does describe the GPIIb promoter, one skilled in the art would not be motivated to use this cell lineage specific promoter in conjunction with the DNA construct disclosed in Hao. Hao used nonspecific viral promoters in his experiments, *see* Hao at p. 875, left col., and does not disclose any data regarding cell lineage specific promoters such as the GPIIb promoter. Hao further discloses that "use of the myeloid or lymphoid-specific promoters would similarly direct gene expression to the phagocytic cells and lymphocytes, respectively." (*Id.* at p. 879, left col.) Direction of gene expression to megakaryocytes is not mentioned. Moreover, Hao is merely speculating that these cell lineage specific promoters might work. Based on this disclosure, one of skill in the art would, at most, be motivated to try to use a myeloid or lymphoid specific promoter in cell lines.

Applicants acknowledge that Hao states that "use of hematopoietic-specific promoters *may* result in persistent *in vivo* expression in the hematopoietic cells. . ." (*Id.* emphasis added.) Conceivably, this disclosure could provide a general incentive to try a hematopoietic specific promoter such as the GPIIb promoter disclosed in Uzan. However, a general incentive does not make obvious a particular result. *In re Deuel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995). Such a general incentive may make an approach "obvious to try" but it does make the invention obvious. "Obvious to try" is not the standard of obviousness under 35 U.S.C. § 103. *In re O'Farrell*, 853 F. 2d 894, 903 (Fed. Cir. 1988).

Further, Hao in view of Uzan does not provide one of skill in the art with a reasonable expectation of successfully transfecting a hematopoietic cell with a DNA construct which includes the GPIIb promoter. Hao describes the *in vitro* expression of FIX in human myeloid

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leukemia cell line. (*Id.* at p. 874, left col.) The myeloid leukemia cell line is not a natural hematopoietic cell but rather, a transformed cell line. As Hao admits, "it is more difficult to achieve consistent expression of exogenous genes in primary, nontransformed cells than in immortal cell lines." (*Id.* at p. 879.) Thus, Hao concedes that expression in nontransformed cell lines is difficult. Accordingly, one of skill in the art would not have a reasonable expectation of successfully transfecting and expressing a DNA construct in a nontransformed hematopoietic cell even if the GPIIb promoter of Uzan is used.

The Office has failed to establish a *prima facie* case of obviousness for at least the reasons stated above. Accordingly, Applicants respectfully request the withdrawal of the rejection of claims 1, 5 , 9 and 10-12.

If there is any fee due in connection with the filing of this Statement, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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Dated: September 17, 2002

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APPENDIX

2. **(TWICE AMENDED)** The DNA-construct as claimed in claim 8, wherein the DNA sequence functioning as a promoter is the DNA sequence coding for **the** human platelet glycoprotein IIb (GPIIb) **promoter**.

8. **(AMENDED)** The DNA-construct according to claim 1 wherein the hematopoietic cells are **[platelets] megakaryocytes**.

12. **(AMENDED)** The process according to claim 9 wherein the DNA sequence functioning as a promoter is the DNA sequence for **the** human platelet glycoprotein IIb (GPIIb) **promoter**.

13. **(AMENDED)** The process according to claim 9 wherein the hematopoietic cells are **[platelets] megakaryocytes**.

14. **(AMENDED)** The process according to claim 5 wherein the hematopoietic cells are **[platelets] megakaryocytes**.

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